ABSTRACT OF THE INVENTION

A simple method for modifying genes in a recombination deficient host cell is disclosed. Such modifications include generating insertions, deletions, substitutions, and/or point mutations at any chosen site in the independent origin based cloning vector. The modified gene is contained in an independent origin based cloning vector that is used to introduce a modified heterologous gene into a cell. Such a modified vector may be used in the production of a germline transmitted transgenic animal, or in gene targeting protocols in eukaryotic cells. In particular, high throughput methodology is provided for generating the modified the independent origin based cloning vectors of the present invention.